Remarks

Formal matters:

Applicants acknowledge that the status claim 5 was mislabeled in the previously filed amendment and thank the Examiner for proceeding with examination of the application. The appropriate status identifiers have been used with this amendment.

Priority

The action states Application Nos. 10/345,021, 10/186,757, and 10/157,654 (now U.S. Patent 7,101,995) fail to provide adequate support for enablement for the claims of the instant invention. Applicants respectfully disagree. Support for a polyvinylamine can be found in U.S. 7,101,995 (issued from U.S. Application 10/186,757) in column 2 lines 21-25 combined with column 14 lines 25-45.

Double Patenting:

Claims 1-3 and 5-9 have been rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 1, 2, 6, and 7 of U.S. Patent 5,744,335 in view of Wolfert et al. (Bioconjugate Chemistry 1999) and Leake et al. (US 2004/0224405). Applicants respectfully disagree. While any polycation of sufficient size will condense plasmid DNA, not every polycation will function as a DNA transfection reagent. Furthermore, a polycation that functions as a good transfection reagent with plasmid DNA will not necessarily function as a good transfection reagent with siRNA (see Meyer M. et al. Human Gene Therapy 17:1062-1076 (2006); page 1071, 1st column, 3rd full paragraph and Declaration filed with Applicants reply of 12/11/2006). Therefore, it could not have been obvious to combine the polyvinylamine of Wolfert et al. with the lipid of '335 to create an siRNA transfection delivery composition. Applicants request reconsideration of the double patenting rejection.

Claims 1-3 have been rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 1-3 of U.S. Patent 7,101,995, in view of both Wolfert et al. and Leake et al. With this reply, Applicants have filed a terminal disclaimer to overcome the rejection.

Claims 1-3 have been rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/845,968. With this reply, Applicants have filed a terminal disclaimer to overcome the rejection.

Rejection of the claims under 35 USC §103:

Claims 5, 6, and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al. (U.S. Patent 5,744,335) in view of Wolfert et al (Bioconjugate Chem. 1999) and Pollard et al. (J Biol Chem, 1998, 27:7507-7511). Applicants have previously argued that polyvinylamine can not be reasonably anticipated to substitute for the histone of '335 to form an effective siRNA delivery composition. The Action states that arguments can not take the place of evidence of record. However, there is no evidence of record to suggest that polyvinylamine together with the amphipathic compound of the instant invention or '335 will form an siRNA delivery agent. In fact, Applicants submitted evidence that, if polyvinylamine is substituted for the histone of '335, the results composition does not form a DNA delivery reagent. It is the Applicants' opinion, that the Examiner is combining teachings that have not been shown to be necessarily related. The ability of a polycation to condense nucleic acid does not prove that the polycation is a good transfection reagent. Similarly, the ability of a polycation to be displaced from DNA following microinjection does not prove that the polycation is a transfection reagent. Finally, the utility of a given polymer to function as a transfection reagent in combination with one set of compounds does not prove that the same polymer will function as a transfection reagent with a second set of compounds. With respect specifically to Wolfert et al., microinjection is not transfection. Microinjection is a mechanical means of injecting a compound directly into a cell. Thus, expression of a DNA following microinjection can not reasonably be considered to be predictive of transfection ability. Applicants reiterate that Wolfert et al. state: polyvinylamine "gave **no** significant spontaneous transfection when applied to 293 cells in vitro" (page 999, 2nd column, 2nd paragraph).

The Action notes on page 14, that the prior art teaches the desirability to target siRNA to the cell nucleus. This statement is incorrect, as siRNA exerts its effects in the cytoplasm on not the nucleus (see Meyer M. et al. Human Gene Therapy 17:1062-1076 (2006); see page 1063, 1st column, 2nd full paragraph, "siRNAs act at the "loss of gene function" level, knocking

down endogenous gene activity. Delivery into the cytosol as the effector site is sufficient, thus avoiding the delivery hurdle of nuclear uptake.")

The Action further states that the data presented in the Declaration filed 12/11/2006 do not pertain to the instant invention. Applicants respectfully disagree. The data presented in the Declaration directly address the obviousness of combining a polyvinylamine, as taught by Wolfert et al., with the teaching a Wolff et al. The Declaration clearly shows that combining the polyvinylamine of Wolfert et al., with the amphipathic compound of Wolff et al., results in a composition that fails to deliver plasmid DNA to a cell (the functional test of Wolff et al.). Thus, one would not have been motivated to combine the teachings of Wolfert et al. and Wolff et al. Therefore, the further extrapolation to combining the teachings of Wolfert et al. and Wolff et al. to the delivery of short siRNA oligonucleotide can not be considered to be obvious.

Applicants request reconsideration of the rejection.

Rejection of the claims under 35 USC §103:

Claims 1-3 and 5-9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al. (U.S. Patent 7,101,995) in view of each Wolfert et al. Pollard et al., and Leake et al. With this reply, Applicants have filed a declaration under 35 C.F.R. 1.132 stating that the disclosed but not claimed in '995 was derived from the inventor of the instant application and is thus not an invention by another.

The Examiner's rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 1-3 and 5-9 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being transmitted to the USPTO on this date: July 2, 2007 .

/Kirk Ekena/
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